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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/818,461	03/27/2001	Benjamin D. Silverman	YOR920000779US2	1831

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Ryan, Mason & Lewis, LLP
1300 Post Road, Suite 205
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EXAMINER

BORIN, MICHAEL L

ART UNIT	PAPER NUMBER
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1631

DATE MAILED: 01/15/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

34.

Office Action Summary

8-11.

Application No.

09/818,461

Applicant(s)

SILVERMAN, BENJAMIN D.

Examiner

Michael Borin

Art Unit

1631

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 23 October 2003.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-43 is/are pending in the application.
- 4a) Of the above claim(s) 4,7-21,25,28-32,36 and 39-43 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-3,5,6,22-24,26,27,33-35,37 and 38 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
* See the attached detailed Office action for a list of the certified copies not received.
- 13) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.
a) ☐ The translation of the foreign language provisional application has been received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892) 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ 6) ☐ Other: _____

Art Unit: 1631

DETAILED ACTION

Status of Claims

1. Claims 1-43 are pending.

Response to restriction requirement filed 10/23/2003 is acknowledged. Applicant elected, with traverse, Group I, claims 1-6,22-27,33-38. Applicant argues that there is no burden of search because all inventions are similarly classified.

For purposes of the initial requirement, a serious burden on the examiner may be prima facie shown if the examiner shows by appropriate explanation either separate classification, separate status in the art, or a different field of search. As explained in the restriction requirement, Group I does not require detecting centroid of protein and detecting distances therefor as required for Groups II, III, and Group III requires step calculating moments of hydrophobicity distribution not required for Groups I,II. Therefore, the groups have separate status in art and require non coextensive search of literature even though their patent classification is the same.

The restriction requirement is still deemed proper and is therefore made FINAL. Claims 7-21, 28-32,39-43 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected groups.

As for election of species requirement, applicant elected species wherein adjusted second order moment of hydrophobicity is determined. Claims 1-3,5,6,22-24,26,27,33-35,37,38 read on elected species, claims 1-3,6,22-24,27,33-35,38

Art Unit: 1631

being generic. Claims 4,25,36 are withdrawn from consideration as being drawn to non-elected species.

Claim Rejections - 35 USC § 112, second paragraph.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

2. Claims 1-3,5,6,22-24,26,27,33-35,37,38 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The rejection is applied for the following reasons.

Claims 1,22,33, and claims dependent therefrom, recite the step of determining hydrophobicity distribution of a protein, which is vague and indefinite. It is not clear whether, the distribution of protein addressed in the claim is in some physical environment, virtual environment, or, as it seems from the specification, is not a distribution of protein at all, but distribution of hydrophobicity throughout the given protein molecule. Please clarify.

Art Unit: 1631

Claims 1,22,33, and claims dependent therefrom, recite the phrase "shifting hydrophobicity distribution" which is vague and indefinite. It is not clear distribution of what, protein or amino acids comprising thereof, is being shifted, is it a shift in space (virtual or physical), or shift in values. Applicant can resolve this issue by particularly pointing out the steps involved the "shifting hydrophobicity distribution", e.g, as disclosed on p. 9, lines 7-8 of specification.

Claim Rejections - 35 U.S.C. § 101

3. Claims 1-3,5,6 are rejected under 35 USC 101 because the claimed invention is drawn to non-statutory subject matter. The invention as claimed is drawn to a series of computational steps towards modifying hydrophobicity values of amino acid constituents of a protein in a modeled virtual environment. The specification discloses mathematical steps used in the method. These steps result in a protein model having zero net hydrophobicity in the virtual environment. There is no "useful, concrete, and tangible result" obtained as a result of the claimed method. If the "acts" of a claimed process manipulate only numbers, abstract concepts or ideas, the acts are not being applied to appropriate subject matter. A process consisting solely of mathematical operates, i.e., converting one set of numbers into another set of numbers, does not manipulate appropriate subject matter and thus can not constitute a statutory process.

Art Unit: 1631

Claim Rejections - 35 USC § 112, first paragraph.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 1-3,5,6,22-24,26,27,33-35,37,38 are rejected under 35 U.S.C. 112, first paragraph, because the specification while being enabling for a computer-driven computational method made on a protein modeled in virtual environment, does not reasonably provide enablement for a method of profiling proteins by physically changing protein's hydrophobicity in a real environment. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The specification appears to disclose a computer program product and computer-implemented method wherein hydrophobicity of amino acid residues comprising the protein of interest are shifted by subtracting the average hydrophobicity from each value of hydrophobicity distribution of each amino acid residue, so that as a result the net hydrophobicity of protein vanishes. The specification appears to indicate that applicant's inventive concept revolves around such specific "shifting" operation, rather than encompasses any broad definition of

Art Unit: 1631

the term "shifting". This is not reflected in the claims. It is noted that the claims are not limited to well-understood computational and/or physico-chemical processes, and the specification does not provide exemplification or guidance on performing method steps in the broad scope they encompass (e.g., determining hydrophobicity of protein in physical, e.g., aqueous, environment, and shifting the hydrophobicity by physical methods). The specification does not appear to disclose suitable algorithms or implementations. There is no evidence of record that implementation of any of these tasks would have been well known or routinely performed by those of ordinary skill in the art at the time of the invention.

In view of the above, it is the Examiners position that with the insufficient guidance and working examples and in view of unpredictability and the state of art one skilled in the art could not make and/or use the invention with the claimed breadth without an undue amount of experimentation.

Claim Rejections - 35 USC § 102 and 103.

The following is a quotation of the appropriate paragraphs of 35 U.S.C.102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Art Unit: 1631

5. Claim 1 is rejected under 35 U.S.C. 102(b) as anticipated by Bar-Or et al (Database CaPlus, DN 103:84898. Archives of Microbiology, 1985, 142(1), pages 21-27).

Instant claim is drawn to method of spatially profiling proteins comprising steps of determining hydrophobicity distribution of a protein and shifting the hydrophobicity distribution.

Bar-Or et al teach method of modulation of cell surface hydrophobicity by treatment of cell surface proteins with proteolytic agents and/or mechanical shearing, or amphenicol. The method includes initial evaluation of hydrophobicity, which reads on instantly claimed step of "determining a hydrophobicity distribution" , and a step of treatment of cell surface which clearly shifts hydrophobicity distribution of a protein (e.g., as a result of treatment with a proteolytic agent).

It is the Examiners position that all the elements of Applicant's invention with respect to the specified claim are instantly disclosed by the teaching of the reference cited above.

6. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michael Borin whose telephone number is (703) 305-4506. Dr. Borin can normally be reached between the hours of 8:30 A.M. to

Serial Number: 09/818461

Page 8

Art Unit: 1631

5:00 P.M. EST Monday to Friday. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mr. Michael Woodward, can be reached on (703) 308-4028. The fax telephone number for this group is (703) 305-3014.

Any inquiry of a general nature or relating the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

December 31, 2003

MICHAEL BORIN, PH.D.
PRIMARY EXAMINER

MICHAEL BORIN, PH.D.
PRIMARY EXAMINER

